REMARKS

I. Detailed Action

A. The Examiner has acknowledged Applicant's election of Group I, claims 1-8, 14-18, and 20-31 with traverse. The Applicant's argument that no separate search is required to search the non-elected groups as all claims are related as product and method of use has been deemed to be non-persuasive. Applicants will cancel all other claims once the claimed invention is in condition for allowance. Applicants acknowledge that the election/restriction has been made FINAL.

B. Applicants thank the Examiner for pointing out the inadvertent mistake of not complying with all of the conditions necessary to receive an earlier filing date under 35 U.S.C. § 119(e). Accordingly, Applicants have now amended the specification to comply with 37 CFR §§ 1.78(a)(2) and (a)(5).

C. Applicants thank the Examiner for pointing out the inadvertent mistake of failing to comply with the sequence rules of 37 CFR §§ 1.821-1.825. Accordingly, Applicants have now amended the specification to comply with these rules.

II. Claim Objections

A. Claims 20 and 21 stand objected to as being duplicate claims under 37 CFR § 1.75 (b). The Examiner notes that "[b]oth claims encompass a transgenic plant containing a DNA construct encoding EF-TU, wherein expression of EF-TU expression increases tolerance to heat and/or drought, in comparison to a corresponding untransformed plant." The Examiner further notes that the difference between "substantially tolerant" and "tolerant", "transformed" and

"transgenic", and "tolerant" and "resistant" is unclear. Applicants have cancelled claim 20, thereby alleviating this rejection.

B. Claim 22 stands objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim under 37 CFR § 1.75(c). The Examiner notes "[c]laim 22 attempts to limit the plant of claim 21 by requiring the DNA construct to comprise a promoter. However, the DNA construct of claim 21 inherently comprises a promoter, since claim 21 indicates that the DNA construct is being expressed." Applicants have amended claim 21 and cancelled claim 22, thereby alleviating this rejection.

III. Claim Rejections – 35 U.S.C. § 112

A. §112, Second Paragraph

Claims 1-8, 14-18, 20, 23 and 27-31 stand rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention under 35 U.S.C. § 112, second paragraph.

Claim 1 stands rejected as being indefinite for use of the term "expressed primarily." The Examiner notes that it is unclear as to whether the protein can be expressed at times other than heat shock. Claim 1 has been amended to remove this language, thereby alleviating the § 112, second paragraph rejection. Claim 14 has also been appropriately amended.

Claim 1 stands rejected as being indefinite for use of the term "high homology." The Examiner notes that it is unclear what the difference is between high homology and other levels of homology. Claim 1 has been amended to remove this language, making the claim definite. Applicants submit that this amendment alleviates the § 112, second paragraph rejection. Claim 14 has also been appropriately amended.

Claim 1 stands rejected as being indefinite for use of the language "chloroplast elongation factor EF-Tu, from E. coli." The Examiner notes that E. coli do not have chloroplasts. Claim 1 has been amended to remove this language, thereby alleviating the § 112, paragraph 2 rejection. Claim 14 has also been appropriately amended.

Claim 1 stands rejected as being indefinite for use of the term "high stringency." The Examiner notes that "[i]t is not clear what hybridization conditions are considered to be highly stringent." Claim 1 has been amended to remove this language and the stringency requirements from the specification have been added, thereby alleviating the § 112, paragraph 2 rejection.

Claim 1 stands rejected as being indefinite for use of the term "(putative coding region)." The Examiner notes it is unclear what this term "adds to the claimed invention." Claim 1 has been amended to remove this language, thereby alleviating the § 112, paragraph 2 rejection.

Claim 1 stands rejected as being indefinite because the Examiner states it is unclear "if the protein encoded by the nucleotide sequence is approximately 45 kD before, or after, import into the chloroplast, if the nucleotide sequence is from a nuclear gene."

Applicants respectfully traverse this rejection. As taught in the specification:

> "[t]ransport of protein produced by transgenes to a subcellular compartment such as the chloroplast, vacuole, peroxisome, glyoxysome, cell wall or mitochondrion, or for secretion into the apoplast, is accomplished by means of operably linking the nucleotide sequence encoding a signal sequence to the 5' and/or 3' region of a gene encoding the protein of interest. Targeting sequences at the 5' and/or 3' end of the structural gene may determine, during protein synthesis and processing, where the encoded protein is ultimately compartmentalized. The presence of a signal sequence directs a polypeptide to either an intracellular organelle or subcellular compartment or for secretion to the apoplast." (specification, p. 23-24)

The specification further teaches in Example 3:

> "[t]he study on protein origin revealed that chloroplast polypeptides of 45 kD were synthesized in the cytosol. The results on subcellular localization and origin of 45 kD polypeptides are, thus, consistent with the sequence data. Combined,

> they suggest that major fraction of 45 kD proteins is chloroplast protein synthesis elongation factor (EF-Tu). . ." (specification, p. 47)

The specification thus teaches that the protein is approximately 45 kD when it is synthesized in the cytosol, before it is imported into the chloroplast. Therefore Applicants submit that the claim is not indefinite under § 112, second paragraph since the specification teaches that the protein is approximately 45 kD prior to its importation into the chloroplast.

Claim 1 stands rejected as being indefinite because the Examiner notes that the claim indicates that the protein is primarily expressed under conditions of heat shock. The Examiner further states it is unclear whether "the isolated nucleotide sequence also comprises a heat inducible promoter."

Applicants respectfully traverse this rejection. As taught in the specification, "in each construct the DNA sequences of interest will preferably be operably linked (i.e., positioned to ensure the functioning of) to a promoter which allows the DNA to be transcribed . . . . Promoters useful for expression in plants are known in the art . . . . Any identifiable promoter may be used in the methods of the present invention which causes expression during stress as defined herein." (specification, p. 19). The specification thus teaches that the nucleotide sequence of claim 1 encodes upon expression the 45 kD protein. As taught in the specification, those skilled in the art would know that a promoter would need to be linked to the nucleotide sequence in order for transcription to occur and which promoters might operatively be linked to the nucleotide sequence in order to express the 45 kD protein under conditions of stress. Therefore Applicants submit that claim 1 is not indefinite under § 112, second paragraph.

Claim 2 stands rejected because the Examiner notes that the claim limits the nucleotide sequence of claim 1 to SEQ ID No:5, which is set forth as an amino acid sequence. Applicants

respectfully acknowledge this objection and have cancelled the claim. Applicants thank the examiner for pointing out this inadvertent mistake.

Claim 3 stands rejected as being indefinite for use of the term "capable of directing expression of a protein." The Examiner states that the term "does not make clear if expression actually occurs, or when or under what conditions." Applicants have amended the claim with the Examiner's suggested language, thereby alleviating the § 112, second paragraph rejection. Applicants wish to thank the Examiner for this suggested language.

Claim 14 stands rejected as being indefinite because the Examiner notes the last recited step and the preamble are inconsistent. The Examiner further notes "the claim is directed to a method for increasing plant tolerance to heat and draught. However, the last recited step results in a transformed cell, not a plant." Applicants have amended the claim with appropriate language to indicate the transformed cells are regenerated to transgenic plants, thereby alleviating the § 112, second paragraph rejection. Applicants wish to thank the Examiner for this suggestion.

Claim 15 stands rejected as having insufficient antecedent basis for the term "said expression cassette." The Examiner notes there is "insufficient basis for this term in the claim or claim 14."

Applicants respectfully traverse this rejection. Applicants respectfully believe that the Examiner has misread the term in Claim 15 as cassette. The term in claim 15 reads "said expression construct elements." As taught in the specification, "[t]ypically, gene expression is placed under the control of certain regulatory elements including promoters, tissue specific regulatory elements, and enhancers" (specification, p. 13). Claim 14 includes the nucleotide sequence being operatively linked to a promoter and other regulatory elements and regions.

Applicants thus submit that there is sufficient antecedent basis for the term "said expression construct elements."

Claim 17 stands rejected for missing a step. The Examiner notes that "claim 17 limits claim 14 by requiring the selection of transgenic plants." The Examiner further notes that with the amendment of claim 14 to indicate that the transformed cells are regenerated to a transgenic plant claim 17 is not further limiting. Applicants have cancelled claim 17, thereby alleviating the § 112, second paragraph rejection.

Claims 20 and 28 stand rejected as being indefinite for use of the term "substantially." The Examiner further notes that "[i]t is not clear what the significance of the term 'substantially' is in the definition."

Applicants respectfully traverse this rejection. An Applicant may be his or her own lexicographer by defining his or her terms in the specification. MPEP § 7.06.03(d). As defined in the specification, substantially tolerant means that a transgenic plant has "tolerance to heat and/or drought conditions that adversely affects cell metabolism, plant growth, and/or development in the corresponding non-transgenic or non-transformed plant" (specification, p. 14). Applicants therefore submit that the claims are not indefinite for the use of the term substantially tolerant since the term is defined in the specification.

Claims 23 and 29 stand rejected as being indefinite. The Examiner notes that "they do not clearly indicate whether the seeds or progeny comprise the DNA construct." Claims 23 and 29 have been amended and clearly indicate whether the seeds or progeny comprise the DNA construct, thereby alleviating the § 112, second paragraph rejection.

Claim 27 stands rejected as being indefinite for use of the term "obtainable." The Examiner states "[i]t is not clear whether or not the plant is obtained, or what other way the plant is obtained." Applicants have amended the claim with the Examiner's suggested language, thereby alleviating the § 112, second paragraph rejection. Applicants wish to thank the Examiner for this suggestion.

B. §112, first paragraph: Written Description

Claims 1, 3-8, 14-18, and 20-31 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse this rejection. "A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption." In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. Id. The Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in Applicants' disclosure a description of the invention defined by the claims. In re Wertheim, 541 F.2d 257, 262 (CCPA 1976). In rejecting claims, the Examiner must set forth express findings of fact regarding the above analysis which support the lack of written description conclusion. Id.

In this case, it is respectfully submitted that the Examiner has not met the initial burden of presenting evidence as to why a person skilled in the art would not recognize in Applicant's disclosure a description of other nucleotide sequences which hybridize under stringent conditions to SEQ ID NO:6 and which encode upon expression a 45 kD protein expressed under heat shock conditions and localized in chloroplast. Instead, the Examiner merely notes that the specification fails to describe a nucleotide sequence other than SEQ ID NO:6 and that because "high homology" and "high stringency" are not defined the structural relationship between the claimed nucleotides and SEQ ID NO:6 are not described.

Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art". Regents of University of California v. Eli Lilly, 119 F.3d 1559, 1569 (Fed. Cir. 1997). Although the specification does not explicitly list all other possible nucleotides, it does state that "[a]ny nucleotide sequence encoding the EF-Tu polypeptides may be used in accordance with the present invention"(specification, p. 15).

In addition, the specification states that "[m]ethods for identifying these and other polynucleotides are known to those of skill in the art and will typically be based on screening for other plants with heat and drought tolerance which express EF-Tu during stress" (specification, p. 15). As stated in the amended claim 1, these polynucleotides must hybridize to SEQ ID No:6 under stringent conditions. The conditions for stringency are defined in the specification:

> "As used herein the term "stringency" shall mean conditions of hybridization equivalent to the following: hybridized for 12 hours at 42°C in a buffer containing 50% formamide, 5 X SSPE, 2% SDS, 10 X Denhardt's solution, and 100 μg/ml salmon sperm DNA, and washing with 0.1 X SSC, 0.1% SDS at 55°C and exposed to Kodak X-Omat AR film for 4 days at -70°C" (specification, p. 14-15).

Due to the stringent hybridization requirements, a person skilled in the art would expect the claimed polynucleotides to be structurally similar.

The combination of the coding function of the claimed polynucleotides in conjunction with the stringent hybridization conditions and the knowledge of those skilled in the art on isolating and identifying claimed polynucleotides make clear that Applicants have adequately described the nucleotide sequences encompassed by the claims.

It is therefore respectfully submitted that the Examiner has failed to meet the requisite burden for showing a violation of the written description requirement. Applicants therefore respectfully request that this ground of rejection be withdrawn.

C. § 112, first paragraph: Enablement

Claims 1, 3-8, 14-18 and 20-31 were rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner states that "[t]he claims(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention."

Applicants respectfully traverse this rejection. The test for enablement under § 112, first paragraph, is "whether or not the specification contains a sufficiently explicit disclosure to enable one having ordinary skill in the relevant field to practice the invention claimed therein without the exercise of undue experimentation." Ex Parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int'f 1986). Several factors may be considered in determining whether a specification is enabling. Although none of these factors are controlling and not all of them need be considered, they are illustrative: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The Examiner states that "the specification does not teach other isolated nucleotide sequences encoding a 45 kD chloroplast protein expressed primarily during heat shock, and having high homology to chloroplast EF-Tu from E.coli or tobacco, or further capable of hybridizing under high stringency conditions to SEQ ID No:6, other than SEQ ID No: 6." The Examiner also cites In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Duel, 34 USPQ2d 1210 (Fed. Cir. 1995) for the proposition that "the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein."

Applicants respectfully traverse this rejection. The specification provides clear guidance as to how other nucleotide sequences which encode EF-Tu might be used in accordance with this invention. As noted in the specification:

> "Methods for identifying these and other polynucleotides are known to those of skill in the art and will typically be based on screening for other plants with heat and drought tolerance which express EF-Tu during stress. Nucleotide sequences encoding this protein are easily ascertainable to those of skill in the art through Genbank or the use of plant protein codon optimization techniques known to those of skill in the art and disclosed in the references disclosed herein (for example see EPO publication number 0682115A1 and Murray et al., 1989, Nuc Acid Res., Vol. 17 No. 2, pp 447-498, "Codon Usage in Plant Genes"" (specification, p. 15-16).

The guidance provided by the specification for identifying nucleotide sequences which are encompassed by the invention is clear and well understood by those skilled in the biotechnology field. The amount of work to identify and ascertain these sequences is low. As described by the specification, those skilled in the art would know to isolate plants which express EF-Tu in times of stress. The nucleotides which encode for this protein would then be easily ascertainable using methods which are well described in the prior art. Furthermore, the specification provides an example which illustrates how a nucleotide sequence (in this example, SEQ ID No:6) encoding for EF-Tu might be identified and isolated by one skilled in the art. (specification, Example 4, p. 50) Thus, given the guidance provided by the specification and the prior art, an individual having ordinary skill in the art would easily be able to practice the invention without a level of undue experimentation.

The Examiner next states that "the specification does not teach that plants transformed with any nucleotide sequence encoding a chloroplast EF-Tu was produced . . . ." The Examiner further notes that it is unpredictable as to whether a transgenic plant which has been transformed

with the claimed nucleotide sequence would show increased drought or heat resistance, since it was not shown that SEQ ID No:6 actually encoded for EF-Tu.

Applicants respectfully traverse this rejection. The specification teaches and confirms that SEQ ID No:6 encodes for EF-Tu. As taught in Example 4 of the specification:

> "We obtained EF-Tu peptide sequence from protein spots showing differential abundance on 2-D gels. The inventors then used this sequence and blasted it against our maize EST database. Multiple ESTs had translated homology with the protein sequence. Upon blasting these ESTs against the public database, it was found that they matched various EF-Tu genes. We selected one clone (CHSTG79R) that had high homology (BLAST Score = 333) with a tobacco chloroplast elongation factor. This EST came from a cDNA library that was constructed from B73 seedlings that were drought and heat stressed" (specification, p. 50)

As further taught in the specification (p. 50), the clone was then sequenced, resulting in SEQ ID No:6. The specification thus shows, that by using methods known to those skilled in the art, SEQ ID No:6 was shown to encode for EF-Tu from a drought and heat resistance plant.

The Examiner next states that "the claim invention encompasses expressing any EF-Tu in transgenic plants, including those that are not localized to the chloroplast or whose expression is not increased during heat or drought conditions." The Examiner further notes that "[t]he specification does not teach that any such EF-Tu proteins are involved in conferring heat or drought resistance."

Applicants respectfully traverse this rejection. The specification teaches that the invention encompasses EF-Tu which is expressed during times of heat and drought stress:

> As used herein the term "EF-Tu" shall be intended to include any of the family of 45 kD heat shock proteins including SEQ ID NOS:1-3, expressed upon heat and drought stress conditions described herein and as exemplified by the maize line ZPBL 1304, and those sequences substantially equivalent thereto" (specification, p. 11).

Furthermore, the specification teaches that EF-Tu confers drought and heat resistance to plants:

> "Synthesis of polynucleotides which encode chloroplast protein synthesis elongation factor EF-Tu stabilizes plants during stress caused by heat and drought by increasing the refolding of unfolded proteins, protecting proteins against thermal denaturation, and by forming complexes with unfolded proteins" (specification, p. 7).

The specification therefore enables one skilled in the art to use and practice the invention by encompassing EF-Tu which is produced in times of heat and drought stress and which confers resistance to such factors.

The Examiner next states that "claim 7 encompasses non-plant host cells transformed with the claimed isolated nucleotide sequence. As the specification teaches that the exemplified EF-Tu of the invention is expressed in chloroplast, it is not clear what function it would have in other eukaryotic cells." The Examiner further notes that "[g]iven the breadth of the claims, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention."

Applicants respectfully traverse this rejection. The specification teaches in Example 5 that EF-Tu can be cloned into E.coli (specification, p. 50-51). Once so cloned, the E.coli exhibited increased resistance to heat stress:

> The results showed that *E. coli* over-expressing maize EF-Tu displayed increased viability after exposure to heat stress (Fig. 5). The number of *E. coli* colonies, that grew at 37°V following heat stress, was 18% higher ($P< 0.038$) in induced cells (cells producing maize EF-Tu) than in non-induced cells (cells not producing maize EF-Tu) (specification, p. 51).

The specification therefore provides clear guidance to one skilled in the art on how EF-Tu might be introduced into E.coli.

Applicants assert that claims 1, 3-8, 14-18, and 20-31 are enabled by the specification provided. Applicants therefore respectfully request reconsideration and the withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

IV. Claim Rejections- 35 U.S.C. § 102

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Murayama et al. The Examiner states that the cited reference "teach a cDNA sequence encoding a 45 kD tobacco chloroplast EF-Tu."

Applicants respectfully traverse this rejection. Through citation, each and every element must be present. Murayama et al. teaches a cDNA sequence encoding the dicot, tobacco chloroplast EF-Tu. However, there is no teaching in Murayama et al., as required by claim 1, that EF-Tu, as defined in the specification, is expressed under heat shock conditions. EF-Tu was only known to have a role in elongating peptides on ribosomes. Murayama et al. does not disclose, nor even suggest, the role maize EF-Tu has in conferring or increasing heat and drought tolerance. The present invention discloses the novel role maize EF-Tu plays in increasing tolerance by increasing the heat stability of chloroplasts.

Therefore, in light of this traversal, Applicants submit the present invention is clearly not anticipated by Murayama et al. Applicants respectfully request reconsideration and withdrawal of the objection under 35 U.S.C. § 102(b).

V. Conclusion

In light of the above remarks, Applicants respectfully assert that claims 1-8, 14-18 and 20-31 are now in condition for allowance. Applicants respectfully request reconsideration and withdrawal of the above rejections.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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